REMARKS

This amendment is responsive to the instant Office Action mailed September 20, 2005. Original claims 1-46 and added claims 47 and 48 are under examination in the present action. All pending claims stand rejected.

In response to the instant Office Action, the Applicant has amended claims 1 and 12. No claims have been canceled and no new claims have been added.

Claim 2 has been amended to correct an antecedent basis problem resulting from a prior amendment of claim 1 which it is dependent thereon.

Applicant states that the above amendments do not introduce new matter.

1. Applicant is grateful for the withdrawal of the finality of the previous Office Action and entry of the amendments submitted on June 28, 2005.

2. Claims 1-48 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner is of the opinion that the amendment of claim 1 submitted June 28, 2005 requiring that the polymer core is "substantially free" of biological agent is not disclosed in the specification. Applicant respectfully disagrees. As stated at pages 15 and 16 of the specification, the microparticle (or otherwise known as the "polymer core" *see* page 13, lines 18 and 19) is formed in a reaction vessel which does not contain biological agent, *see* page 15, lines 5-29. The "polymer

core" is then "micronized", *see* page 15, line 31, "purified", *see* page 15, line 35, and the "sodium salt thereof" is formed, *see* page 15, lines 35-37. The polymer salt is thereafter "lyophilized", *see* page 16, line 20 and "purified", *see* page 16, line 22. The formed microparticle (or polymer core) salt is then "dispersed in solutions containing the free-base of a [biologically-active] agent", *see* page 17, lines 1 -2. As further stated, "[the] size of the microparticle (or polymer core) plays a role" in the amount of a biological agent that can be immobilized since "the smaller the size of the microparticle (or polymer core) the more ***surface*** area… thus,… more [biological agent] can be immobilized." Although the phrase "substantially free of peptide, protein or a combination there of" is not specifically found in the specification, it is clear from a careful reading thereof by one of skill in the art that the polymer core is inherently free of biological agent.

Although Applicant does not agree with the Examiner and respectfully requests that the Examiner reconsider this rejection, in an effort solely to put this application in a condition for allowance, Applicant has amended claim 1 to remove the requirement that the polymer core be substantially free from of peptide, protein or a combination thereof.

Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-48 under 35 U.S.C. §112, first paragraph.

3. Claims 1-48 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner is of the opinion that the part of the microparticle that is the subsurface and the part that is the core is unclear. The Examiner's comments indicate that he mistakenly is of the opinion that the microparticle and the polymer core are two different entities. This opinion is incorrect. As stated on page 13, lines 18-19, the "polymer core" is ***another way*** of referring to microparticles, which as noted on page 13, lines 8-10 "refers to the particles of absorbable polyester, which are preferably in essentially spherical form." As such, the subsurface is part of the polymer core and is just under the surface of the microparticle which is the polymer core. The Examiners statement that "[b]oth the subsurface and the core are below the surface" demonstrates a careless reading of the application since the surface referred to in the claims is the surface of the microparticle or polymer core. Without conceding the correctness of the Examiner's rejection, however, and in an effort solely to advance this prosecution to an allowance, "subsurface" has been replaced with its definition, as found on page 14, lines 6-7, "crevices found on the surface".

Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-48 under 35 U.S.C. §112, second paragraph.

4. Claims 1-22, 22, 23, 26-33 and 47 stand rejected under 35 U.S.C. §103(a) as unpatentable over Shalaby *et al.* (U.S. 5,672,659) or Ignatious *et al.* (WO 97/39738) in view of Shalaby (U.S. 5,612,052) and Chesterfield *et al.* (U.S. 5,366,756).

The microparticles of the instant application are formed by a reaction that takes place in a heterogeneous system involving primarily surface complexes." As correctly noted by the Examiner, both Shalaby *et al.* ('659) and Ignatious *et al.* "disclose a composition containing a carboxyl group-containing polymer that can be a heterochain polymer ***ionically conjugated*** (col. 2, line 65 of Shalaby *et al.* and page 1, line 23 of Ignatious *et al.*) with a bioactive polypeptide or a drug that is a polypeptide." Clearly, as noted by the Examiner, the Shalaby *et al.* ('659) and Ignatious *et al.*, compositions are inconsistent with the complexes of the instant application.

As noted by Ignatious *et al.*, on page 8, lines 16 - 20, "[t]he present invention provides a new pharmaceutical composition that chemically bonds a biocompatible biodegradable polyester to…[a] peptide[] as a ***homogenous*** ionic species" as compared to microparticles of the instant application which clearly are not homogeneous since, as stated on page 5, lines 8-11, "the formation takes place in

a heterogeneous system." The Shalaby *et al.* ('659) compositions are also referred to as "homogeneous ionic species", *see*, col. 4, line 56.

How could a complex in which the peptide is bound to the surface of a polymer core be considered "homogenous"?

Both Shalaby *et al.*('659) and Ignatious *et al.* are directed to ***conjugates*** whereas it is clearly the intent of the instant application to provide an alternative to such conjugates. In the paragraph that spans the end of page 4 and begins on page 5 of the instant application, the Applicant discusses the limitations of the prior art sustained release pharmaceutical compositions indicating that "[the prior art compositions formed by] conjugating carboxylic entities, ionically, with [a] basic polypeptide...form a ***well defined ion-conjugate as a new chemical entity with physiochemical properties***... [which can be] distinguished from the present invention where the **complex** formation takes place in a heterogeneous system involving primary surface complex formation." From this statement it is clear that the components of the microparticles of the instant application maintain their individual physiochemical characteristics. Ignatious *et al.*, in contrast, states at page 8, lines 20-23 that "[b]y chemically bonding polyesters of different molecular weights to the therapeutic agents, ***the chemical characteristics of the composition can be more precisely tailored.***" Shalaby *et al.* ('659), as well, in Fig 2. depicts "[a] molecular

conjugate depicting the ***chemical interactions*** between the lactide/glycolide (malic type) copolymer and Somatuline" wherein "the **chemical characteristics of the composition** can be more precisely tailored to meet the demands for the controlled monophasic release of the biologically active polypeptide molecule *in vivo*." From these statements, it would be clear to one skilled in the art, that the conjugates described by Shalaby *et al.* ('659) and Ignatious *et al.* produce ***new chemical entities*** wherein the parts, i.e., the polyester and the drug, lose their individual physiochemical characteristics. As such, the compositions described in both Shalaby *et al.* ('659) and Ignatious *et al.* are distinguishable from the instant invention. Neither of the secondary references, Shalaby {'052) or Chesterfield, suggest the non-conjugates of the instant application.

In an effort solely to advance the prosecution of the instant application and to better distinguish the instant claims over the teachings in the prior art cited by the Examiner, claims 1 and 12 have been amended to indicate that the biological agent is immobilized on and not conjugated to the polymer core.

Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1-22, 22, 23, 26-33 and 47 stand rejected under 35 U.S.C. §103(a) as unpatentable over Shalaby *et al.* (U.S. 5,672,659) or Ignatious *et al.* (WO 97/39738) in view of Shalaby (U.S. 5,612,052) and Chesterfield *et al.* (U.S. 5,366,756).

5. Claims 12-21, 24, 25, 34-46 and 48 stand rejected under 35 U.S.C. §103(a) as unpatentable over Auer *et al.* (WO 92/11844) in view of Demian *et al.* (U.S. 5,795,922).

Applicant contends that since these claims are dependent upon base claims patentable under 35 U.S.C. §103(a), as noted above, these claims would also be considered to meet the requirements of 35 U.S.C. §103(a).

Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 12-21, 24, 25, 34-46 and 48 stand rejected under 35 U.S.C. §103(a) as unpatentable over Auer *et al.* (WO 92/11844) in view of Demian *et al.* (U.S. 5,795,922).

CONCLUSION

Reconsideration of the instant Office Action and the allowance of all pending claims are respectfully requested. Prompt and favorable action is solicited.

Should Examiner Naff deem that any further action by the Applicants would put this application in order for acceptance, he is invited to telephone Applicant(s) attorney at (508) 478-0144 to facilitate prosecution of this application.

With the exception of the fee for the Petition for a three months extension under 37 C.F.R. §1.136(a), Applicant believes that no fees are due with this response; the Commissioner is, however, hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-0590.

Respectfully submitted,

Date:
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